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TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

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NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 DEC 23 New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
USPAT2
NEWS 4 JAN 13 IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 5 JAN 13 New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
INPADOC
NEWS 6 JAN 17 Pre-1988 INPI data added to MARPAT
NEWS 7 JAN 17 IPC 8 in the WPI family of databases including WPIFV
NEWS 8 JAN 30 Saved answer limit increased
NEWS 9 FEB 21 STN AnaVist, Version 1.1, lets you share your STN AnaVist
visualization results
NEWS 10 FEB 22 The IPC thesaurus added to additional patent databases on STN
NEWS 11 FEB 22 Updates in EPFULL; IPC 8 enhancements added
NEWS 12 FEB 27 New STN AnaVist pricing effective March 1, 2006
NEWS 13 FEB 28 MEDLINE/LMEDLINE reload improves functionality
NEWS 14 FEB 28 TOXCENTER reloaded with enhancements
NEWS 15 FEB 28 REGISTRY/ZREGISTRY enhanced with more experimental spectral
property data
NEWS 16 MAR 01 INSPEC reloaded and enhanced
NEWS 17 MAR 03 Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18 MAR 08 X.25 communication option no longer available after June 2006
NEWS 19 MAR 22 EMBASE is now updated on a daily basis
NEWS 20 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21 APR 03 Bibliographic data updates resume; new IPC 8 fields and IPC
thesaurus added in PCTFULL
NEWS 22 APR 04 STN AnaVist \$500 visualization usage credit offered
NEWS 23 APR 12 LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24 APR 12 Improved structure highlighting in FQHIT and QHIT display
in MARPAT
NEWS 25 APR 12 Derwent World Patents Index to be reloaded and enhanced during
second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
<http://download.cas.org/express/v8.0-Discover/>

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04/23/2006 1030665.trn

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 12:21:30 ON 23 APR 2006

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 12:21:42 ON 23 APR 2006

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STRUCTURE FILE UPDATES: 21 APR 2006 HIGHEST RN 881539-69-1

DICTIONARY FILE UPDATES: 21 APR 2006 HIGHEST RN 881539-69-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

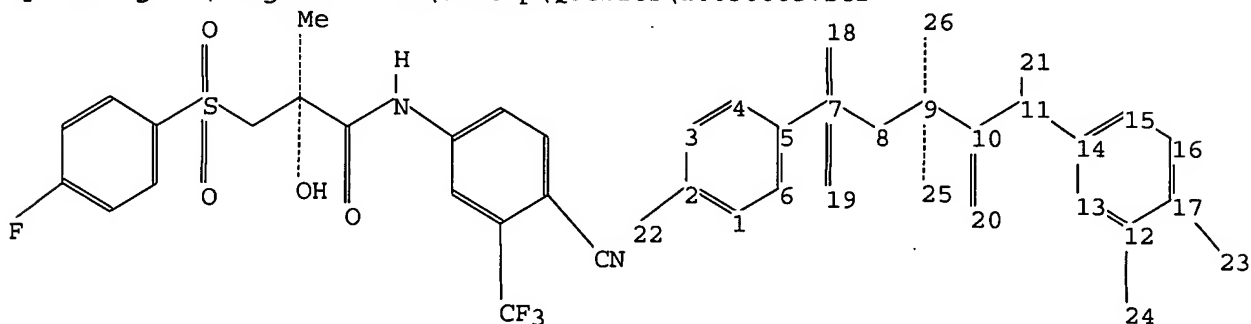
Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10030665.str



chain nodes :

7 8 9 10 11 18 19 20 21 22 23 24 25 26

ring nodes :

1 2 3 4 5 6 12 13 14 15 16 17

chain bonds :

2-22 5-7 7-8 7-18 7-19 8-9 9-10 9-25 9-26 10-11 10-20 11-14 11-21
12-24 17-23

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17

exact/norm bonds :

5-7 7-8 7-18 7-19 9-25 9-26 10-11 10-20 11-14

exact bonds :

2-22 8-9 9-10 11-21 12-24 17-23

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17

isolated ring systems :

containing 1 : 12 :

Match level :

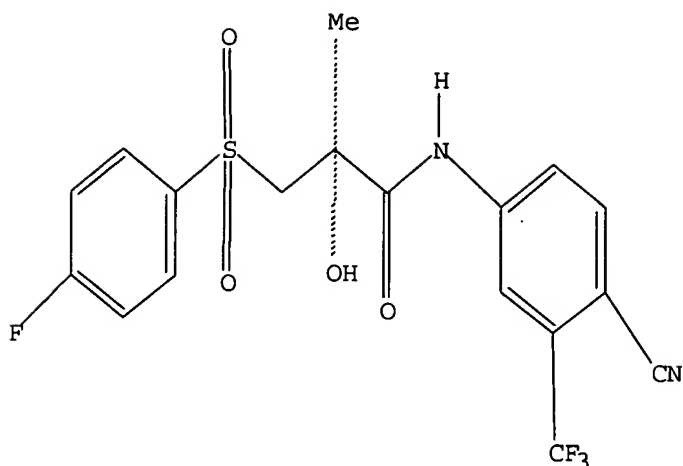
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 12:21:59 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1 TO 80
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 12:22:06 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 44 TO ITERATE

100.0% PROCESSED 44 ITERATIONS
SEARCH TIME: 00.00.01

7 ANSWERS

L3 7 SEA SSS FUL L1

=> FIL HCAPLUS

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	166.94	167.15

FILE 'HCAPLUS' ENTERED AT 12:22:12 ON 23 APR 2006
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FILE COVERS 1907 - 23 Apr 2006 VOL 144 ISS 18
FILE LAST UPDATED: 21 Apr 2006 (20060421/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s 13
L4      558 L3

=> s 14 and process
      2230567 PROCESS
      1508268 PROCESSES
      3328775 PROCESS
          (PROCESS OR PROCESSES)
L5      37 L4 AND PROCESS

=> s 15 and thionyl chloride
      14256 THIONYL
      2 THIONYLS
      14258 THIONYL
          (THIONYL OR THIONYLS)
      1072123 CHLORIDE
      156700 CHLORIDES
      1143870 CHLORIDE
          (CHLORIDE OR CHLORIDES)
      13439 THIONYL CHLORIDE
          (THIONYL(W) CHLORIDE)
L6      1 L5 AND THIONYL CHLORIDE

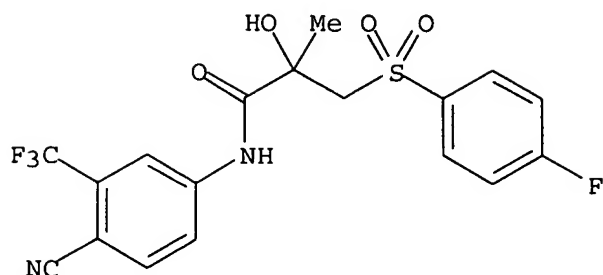
=> s 15 and py<=1999
      19944486 PY<=1999
L7      4 L5 AND PY<=1999

=> d 16 ibib abs hitstr tot
```

```
L6  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:  2005:141019  HCAPLUS
DOCUMENT NUMBER:   142:240198
TITLE:             Process for production of
                   N-methacryloyl-4-cyano-3-trifluoromethylaniline,
                   method for stabilization of the same, and
                   process for production of bicalutamide
INVENTOR(S):       Sugi, Kiyoshi; Shintaku, Tetsuya; Katsura, Tadashi;
                   Itaya, Nobushige
PATENT ASSIGNEE(S): Sumitomo Chemical Company, Limited, Japan
SOURCE:            PCT Int. Appl., 28 pp.
                   CODEN: PIXXD2
DOCUMENT TYPE:     Patent
LANGUAGE:          Japanese
```

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014531	A1	20050217	WO 2004-JP11800	20040811
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2005060302	A2	20050310	JP 2003-292498	20030812
PRIORITY APPLN. INFO.:			JP 2003-292498	A 20030812
OTHER SOURCE(S):			CASREACT 142:240198	
AB	<p>A process for the production of N-methacryloyl-4-cyano-3-trifluoromethylaniline comprises reacting 4-cyano-3-trifluoromethylaniline with methacrylic acid or a reactive derivative thereof in the presence of a polymerization inhibitor; a process for the production of bicalutamide comprises reacting 4-cyano-3-trifluoromethylaniline with <u>methacrylic acid</u> or a reactive derivative thereof in the presence of a polymerization inhibitor and reacting the obtained N-methacryloyl-4-cyano-3-trifluoromethylaniline with a peroxycarboxylic acid, 4-fluorothiophenol, and a peroxycarboxylic acid successively; and a method for the stabilization of N-methacryloyl-4-cyano-3-trifluoromethylaniline comprises incorporating a polymerization inhibitor into N-methacryloyl-4-cyano-3-trifluoromethylaniline. Thus, treatment of methacrylic acid in DMF with thionyl chloride in the presence of 2,6-di-tert-butyl-4-methylphenol (polymerization inhibitor), followed by reaction with 4-cyano-3-trifluoromethylaniline, gave N-methacryloyl-4-cyano-3-trifluoromethylaniline in 89% yield.</p>			
IT	<p>90357-06-5P, Bicalutamide RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (process for production of N-methacryloyl-4-cyano-3-trifluoromethylaniline by reaction of 4-cyano-3-trifluoromethylaniline with methacrylic acid derivative method for stabilization of said aniline derivative and process for production of bicalutamide)</p>			
RN	90357-06-5 HCAPLUS			
CN	Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)			



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 17 ibib abs hitstr tot

L7 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:92156 HCAPLUS

DOCUMENT NUMBER: 133:3008

TITLE: Prostate cancer: molecular biology of early progression to androgen independence

AUTHOR(S): Sadar, M. D.; Hussain, M.; Bruchovsky, N.

CORPORATE SOURCE: British Columbia Cancer Agency, Department of Cancer Endocrinology, Vancouver, BC, V5Z 4E6, Can.

SOURCE: Endocrine-Related Cancer (1999), 6(4), 487-502

CODEN: ERCAE9; ISSN: 1351-0088

PUBLISHER: Society for Endocrinology

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with 109 refs. To improve the therapy for prostate cancer, it will be necessary to address the problems of progression to androgen independence and the **process** of metastatic spread of tumor. The complexity of the latter condition is likely to mitigate against the immediate development of relevant therapeutic approaches. However, the basis of androgen independence appears to be a problem of simpler dimensions and more amenable to treatment with current therapeutic technol. Since early tumor progression can be detected by an incomplete prostate-specific antigen (PSA) response to androgen withdrawal therapy, a study of the mol. biol. of PSA gene regulation may well provide insight into new methods for preventing or delaying this problem. Mounting evidence suggests that ligand-independent activation of the androgen receptor may be one underlying mechanism of androgen independence. In the absence of androgen, a compensatory increase in the activity of cAMP-dependent protein kinase (PKA) enhances the ability of the androgen receptor to bind to the response elements regulating PSA gene expression. The activation of the androgen receptor through upregulation of the PKA signal transduction pathway involves the amino-terminus of the androgen receptor, the function of which may be altered either by modifications such as phosphorylation, or through interactions with co-regulators or other proteins. Of therapeutic interest is the fact that this effect can be counteracted exptl. by the anti-androgen, bicalutamide, and clin. by several other similar agents. We speculate that the inhibition of PKA-activated androgen receptor might also be accomplished by decoy mols. that can bind to the relevant activated site on the amino-terminus or competitively interact with proteins recruited by the PKA pathway that are

responsible for activating the receptor in the absence of androgen. Such mols. might include small mimetic substances or agents that can gain access to the nucleus of the cell.

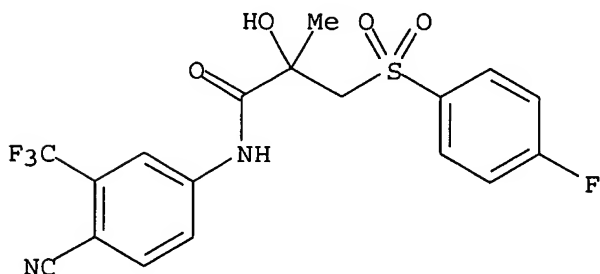
IT 90357-06-5, Bicalutamide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prostate cancer mol. biol. of early progression to androgen independence)

RN 90357-06-5 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 109 THERE ARE 109 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:743995 HCAPLUS

DOCUMENT NUMBER: 130:134291

TITLE: Neoadjuvant hormone therapy before surgery for prostate cancer: the Italian experience (PROSIT study)
AUTHOR(S): Pagano, F.; Bono, A.; Zattoni, F.; Montironi, R.; Galetti, T. Prayer

CORPORATE SOURCE: The Prosit Study Group, Department of Urology, University of Padova, Italy

SOURCE: Molecular Urology (1998), 2(3), 189-194

CODEN: MOURFE; ISSN: 1091-5362

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Despite the growing use in clin. practice of neoadjuvant hormone therapy (NHT) for patients with clin. localized prostate cancer eligible for radical retropubic prostatectomy (RRP), to the authors' knowledge, no randomized trial has addressed the issue of NHT for 6 mo compared with 3 mo and a control arm. It seems worthwhile to determine NHT efficacy in a randomized multicenter trial, testing the efficacy of total androgen blockade (TAB) for 3 or 6 mo in patients with clin. localized prostate cancer (Stage B [AUS/T2N0M0; UICC 1992] or Stage C [T3N0M0]) eligible for radical retropubic prostatectomy 238 patients had been enrolled, and following the randomization process, 82 patients were included in the immediate-surgery arm (Surgery), 77 in the 12-wk NHT arm (12 NHT), and 79 in the 24-wk NHT arm (24 NHT). In both of the NHT treatment arms, there was a trend to a reduction of clin. understaging in clin. Stage B tumors and an increase of clin. overstaging in clin. Stage C tumors. When primary Gleason grade was compared with the final grade in the treated

tumors, there was an apparent higher grade in the surgical than the biopsy specimens. Preliminary results show a better effect of NHT on Stage B tumors.

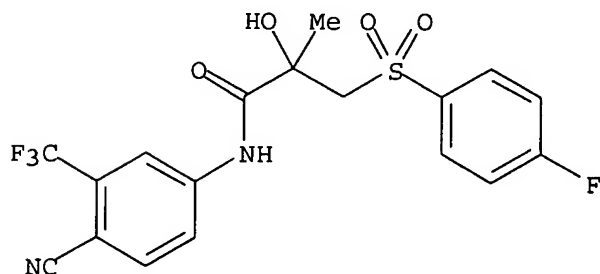
IT 90357-06-5, Bicalutamide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neoadjuvant hormone therapy before surgery for prostate cancer in humans)

RN 90357-06-5 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:950238 HCAPLUS

DOCUMENT NUMBER: 123:330228

TITLE: Ligand-induced conformational alterations of the androgen receptor analyzed by limited trypsinization. Studies on the mechanism of antiandrogen action

AUTHOR(S): Kuil, Cor W.; Berrevoets, Cor A.; Mulder, Eppo

CORPORATE SOURCE: Dep. Endocrinol. Reproduction, Erasmus Univ. Rotterdam, Rotterdam, 3000 DR, Neth.

SOURCE: Journal of Biological Chemistry (1995), 270(46), 27569-76

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Limited proteolysis of in vitro produced human androgen receptor was used to probe the different conformations of the receptor after binding of androgens and several antiandrogens. The results provide evidence for five different conformations of the receptor, as detected by the formation of proteolysis resisting fragments: (1) an initial conformation of the unoccupied receptor not resisting proteolytic attack; and receptor conformations characterized by (2) a 35-kDa proteolysis resisting fragment spanning the ligand binding domain and part of the hinge region, obtained with most antagonists, and in an initial step after agonist binding; (3) a 29-kDa proteolysis resisting fragment spanning the ligand binding domain, obtained in the presence of agonists after an activation process; (4) and (5) 30- and 25-kDa fragments, derived from 2 and 3, but missing part of the C terminus, obtained with RU 486 (RU 486 has antiandrogenic properties, besides its effects as an antiprogesterone/antiglucocorticoid).

Concomitantly with the change from 2 to 3 (and of 4 to 5 for RU 486), dissociation of the 8 S complex of receptor with associated proteins occurred. With a mutant receptor (LNCaP cell mutation in C-terminal region), some antagonists activated transcription analogous to agonists, and induced the activated receptor conformation 3. A mutant lacking the C-terminal 12 amino acids bound RU 486 but not androgens, and formed with RU 486 conformation 5. These data imply that, after the initial rapid binding of ligand, androgens induce a conformational change of the receptor, a **process** that also involves release of associated proteins. RU 486 induces an inappropriate conformation of the C-terminal end, similar as found for its effect on the progesterone receptor. In contrast, the other antiandrogens act at a different step in the mechanism of action: they do not induce an abnormal conformation, but act earlier and prevent a conformation change by stabilizing a complex with associated proteins.

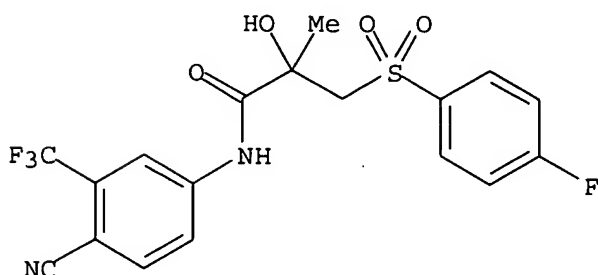
IT 90357-06-5, ICI 176334

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(antiandrogen mechanism of action in relation to ligand-induced androgen receptor conformational alterations)

RN 90357-06-5 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



L7 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:99546 HCAPLUS

DOCUMENT NUMBER: 116:99546

TITLE: Anti-androgens and the mutated androgen receptor of LNCaP cells: differential effects on binding affinity, heat-shock protein interaction, and transcription activation

AUTHOR(S): Veldscholte, Jos; Berrevoets, Cor A.; Brinkmann, Albert O.; Grootegeed, J. Anton; Mulder, Eppo

CORPORATE SOURCE: Dep. Endocrinol. Reprod., Erasmus Univ., Rotterdam, 3000 DR, Neth.

SOURCE: Biochemistry (1992), 31(8), 2393-9

CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Previous studies have shown that LNCaP prostate tumor cells contain an androgen receptor (AR) with a point mutation in the steroid-binding domain (codon 868, Thr to Ala). This defect leads to a change in specificity of the AR. Estrogens, progestagens, and some antiandrogens (e.g., cyproterone acetate, hydroxyflutamide, nilutamide) stimulate LNCaP cell growth rate through the AR. The present studies indicate, that not all

antiandrogens showed agonistic effects with the mutated receptor. The growth rate of LNCaP cells did not increase with the antiandrogen ICI 176,334, nor could this compound increase transcription activation of the reporter gene construct via the mutant receptor in a cotransfection system [HeLa cell cotransfection system with an androgen-regulated reporter gene construct (pG29G-tk-CAT) and the mutant receptor as trans-vector]. Interaction of the AR of LNCaP cells with heat-shock proteins was studied by isolation of the receptor with a specific monoclonal antibody and characterization of associated proteins. Hsp90, hsp70, and hsp56 copptd. with the AR. Incubation of the cells at 37° with androgen (R 1881, 10 nM) or the antiandrogen hydroxyflutamide, prior to receptor isolation, resulted in dissociation of the AR-heat-shock protein complex. This

dissociation

is paralleled by the transformation to a tight nuclear-binding form of the AR. In contrast, ICI 176,334 could not induce a release of heat-shock proteins and did not increase nuclear binding, but inhibited the transformation **process** induced by R 1881. A mechanism of action of antiandrogens in LNCaP cells is proposed in which these compds. affect different steps in the **processes** of receptor transformation and transcription activation. In LNCaP cells, ICI 176,334 shows decreased affinity for the AR and affects steps before DNA binding occurs. In contrast, other antiandrogens including hydroxyflutamide show increased affinity for the mutant AR, affect receptor transformation to the DNA-binding state, and permit interaction of the receptor with the transcription machinery.

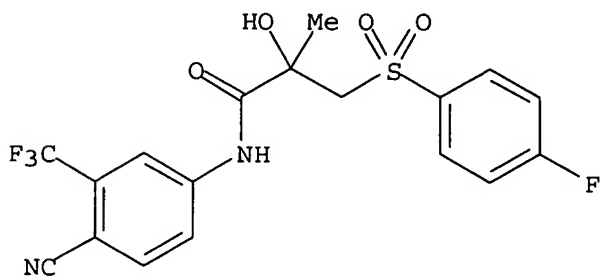
IT 90357-06-5, ICI 176334

RL: PRP (Properties)

(antiandrogen action mechanism of, in prostate tumor cells, receptor transformation and transcription activation in relation to)

RN 90357-06-5 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



=> FIL REGISTRY

COST IN U.S. DOLLARS

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE	TOTAL
ENTRY	SESSION
60.97	228.12
SINCE FILE	TOTAL
ENTRY	SESSION
-3.75	-3.75

FILE 'REGISTRY' ENTERED AT 12:30:28 ON 23 APR 2006

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STRUCTURE FILE UPDATES: 21 APR 2006 HIGHEST RN 881539-69-1
DICTIONARY FILE UPDATES: 21 APR 2006 HIGHEST RN 881539-69-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

```
*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
*****
```

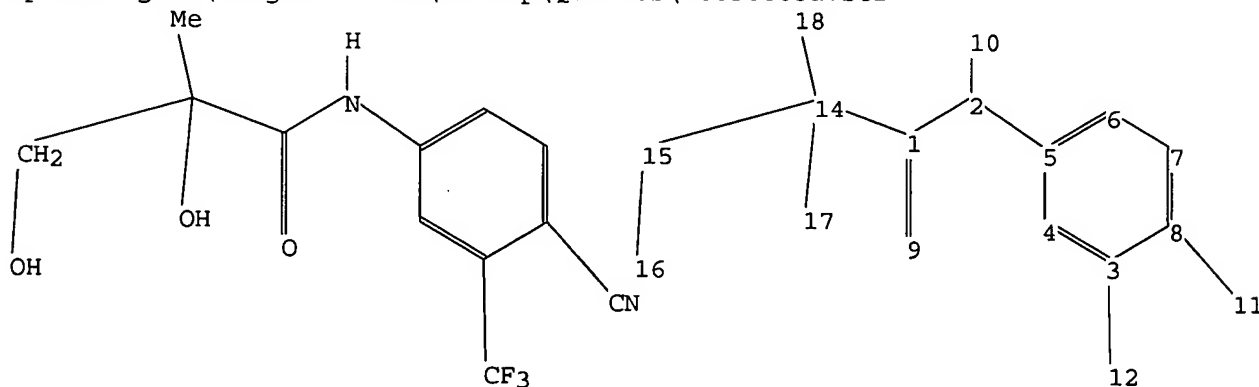
Structure search iteration limits have been increased. See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10030665a.str



chain nodes :

1 2 9 10 11 12 14 15 16 17 18

ring nodes :

3 4 5 6 7 8

chain bonds :

1-9 1-2 1-14 2-5 2-10 3-12 8-11 14-15 14-17 14-18 15-16

ring bonds :

04/23/2006 1030665.trn

3-4 3-8 4-5 5-6 6-7 7-8
exact/norm bonds :
1-9 1-2 2-5 14-17
exact bonds :
1-14 2-10 3-12 8-11 14-15 14-18 15-16
normalized bonds :
3-4 3-8 4-5 5-6 6-7 7-8
isolated ring systems :
containing 3 :

Match level :

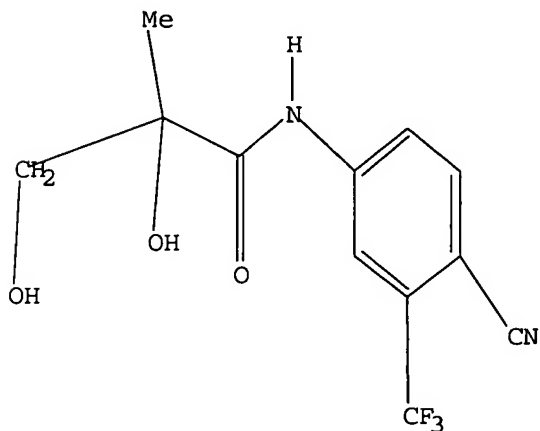
1:CLASS 2:CLASS 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

L8 STRUCTURE UPLOADED

=> d 18

L8 HAS NO ANSWERS

L8 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 18

SAMPLE SEARCH INITIATED 12:30:47 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 11 TO ITERATE

100.0% PROCESSED 11 ITERATIONS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 22 TO 418

PROJECTED ANSWERS: 0 TO 0

0 ANSWERS

L9 0 SEA SSS SAM L8

04/23/2006 1030665.trn

=> s l8 sss full
FULL SEARCH INITIATED 12:30:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 283 TO ITERATE

100.0% PROCESSED 283 ITERATIONS
SEARCH TIME: 00.00.01

3 ANSWERS

L10 3 SEA SSS FUL L8

=> FIL HCAPLUS
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
166.94	395.06

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-3.75

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FILE COVERS 1907 - 23 Apr 2006 VOL 144 ISS 18
FILE LAST UPDATED: 21 Apr 2006 (20060421/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l10
L11 5 L10

=> d his

(FILE 'HOME' ENTERED AT 12:21:30 ON 23 APR 2006)

FILE 'REGISTRY' ENTERED AT 12:21:42 ON 23 APR 2006
STRUCTURE UPLOADED

L1
L2 0 S L1
L3 7 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 12:22:12 ON 23 APR 2006

L4 558 S L3
L5 37 S L4 AND PROCESS
L6 1 S L5 AND THIONYL CHLORIDE
L7 4 S L5 AND PY<=1999

FILE 'REGISTRY' ENTERED AT 12:30:28 ON 23 APR 2006

L8 STRUCTURE UPLOADED
L9 0 S L8
L10 3 S L8 SSS FULL

FILE 'HCAPLUS' ENTERED AT 12:30:59 ON 23 APR 2006

L11 5 S L10

=> s l4 and l11

L12 5 L4 AND L11

=> s l5 and l11

L13 3 L5 AND L11

=> d l13 ibib abs hitstr tot

L13 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:293441 HCAPLUS

DOCUMENT NUMBER: 140:303414

TITLE: **Process** for making bicalutamide and intermediates thereof

INVENTOR(S): Thijs, Lambertus; Keltjens, Rolf; Ettema, Gerrit J. B.
PATENT ASSIGNEE(S): Neth.

SOURCE: U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U.S. Ser. No. 261,492.

CODEN: USXXCO

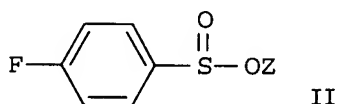
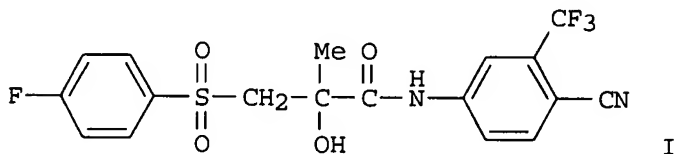
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

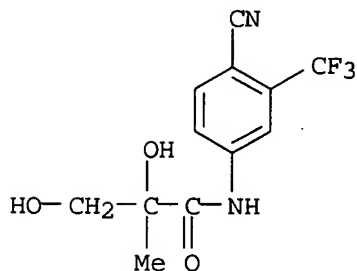
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004068135	A1	<u>20040408</u>	US 2003-682530	20031010
US 2003073742	A1	20030417	US 2002-261492	20021002
<u>US 6818766</u>	B2	20041116		
PRIORITY APPLN. INFO.:			US 2002-261492	A2 20021002
OTHER SOURCE(S):		MARPAT 140:303414		
GI				



AB Bicalutamide (I) and/or its intermediates are made by reaction of p-fluorobenzenesulfinic acid salt (II; Z = a cation) with 2-hydroxyisobutyric acid derivs. of formula YCH₂C(Me)(OX)COA (A = OR;

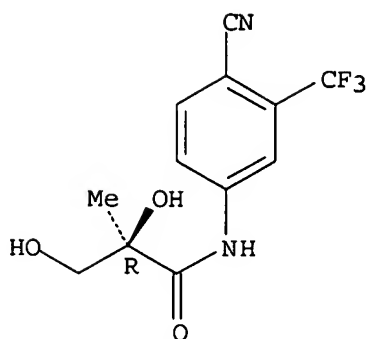
wherein R = H, C1-6 alkyl, C3-6 cycloalkyl, Ph, benzyl, 4-cyano-3-trifluoromethylanilino; Y = leaving group and X = H; or X and Y are joined together to form a 3- to 6-membered heterocyclic ring, in particular oxirane ring; or X and A are joined together to form a 5- to 10-membered fused or unfused heterocyclic ring with the proviso that if a ring nitrogen is present, it may be substituted by a 3-trifluoromethyl-4-cyanophenyl group), YCH₂CMe:CH₂ (Y = same as above), or YCH₂CMe (Y = same as above). Thus, 0.500 g N-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl-2-oxiranecarboxamide (III) was dissolved in dissolved in a mixture of 40 mL CHCl₃ and 40 mL H₂O, successively treated with 371 mg sodium p-fluorobenzenesulfinate and 298 mg tetrabutylammonium bromide, and refluxed for 96 h to give, after workup and silica gel chromatog., 380 mg I (48% yield). Similarly, chiral (R)-I was obtained using chiral epoxide (S)-III in 43% yield.

IT **316373-92-9P**, N-[4-Cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methylpropanamide **316373-93-0P**, N-[4-Cyano-3-(trifluoromethyl)phenyl]-(2R)-2,3-dihydroxy-2-methylpropanamide **316373-94-1P**, (2S)-N-[4-Cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methylpropanamide
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of bicalutamide by coupling of N-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl-2-oxiranecarboxamide or -3-(halo or mesyloxy)-2-hydroxy-2-methylpropanamide with sodium p-fluorobenzenesulfinate)
 RN 316373-92-9 HCAPLUS
 CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl- (9CI) (CA INDEX NAME)



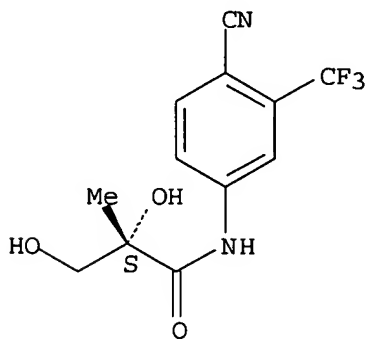
RN 316373-93-0 HCAPLUS
 CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



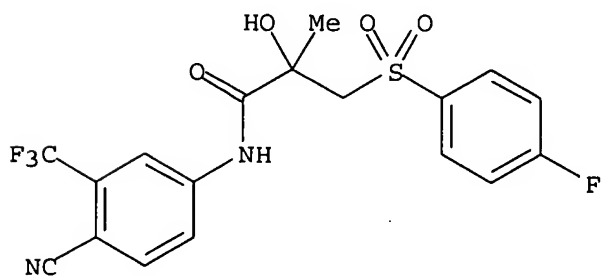
RN 316373-94-1 HCAPLUS
 CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 90357-06-5P, Bicalutamide 113299-40-4P, (R)-Bicalutamide
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of bicalutamide by coupling of N-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl-2-orixanecarboxamide or -3-(halo or mesyloxy)-2-hydroxy-2-methylpropanamide with sodium p-fluorobenzenesulfinate)

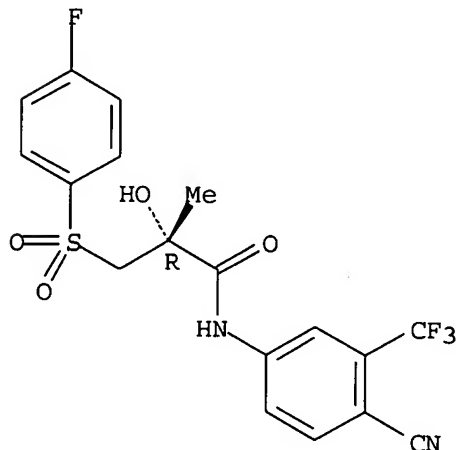
RN 90357-06-5 HCAPLUS
 CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



RN 113299-40-4 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L13 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:511288 HCAPLUS

DOCUMENT NUMBER: 139:85122

TITLE: **Process** for preparing bicalutamide and crystals thereof

INVENTOR(S): Shintaku, Tetsuya; Katsura, Tadashi; Itaya, Nobushige

PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053920	A1	<u>20030703</u>	WO 2002-JP13058	20021213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2469594	AA	20030703	CA 2002-2469594	20021213
AU 2002354475	A1	20030709	AU 2002-354475	20021213
EP 1462442	A1	20040929	EP 2002-788815	20021213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002014933	A	20041214	BR 2002-14933	20021213
US 2003191337	A1	20031009	US 2003-362410	20030224
US 6740770	B2	20040525		

US 2004133031	A1	20040708	US 2003-740140	20031218
ZA 2004004891	A	20050621	ZA 2004-4891	20040621
PRIORITY APPLN. INFO.:			JP 2001-380686	A 20011213
			JP 2002-166213	A 20020606
			WO 2002-JP13058	W 20021213
			US 2003-362410	A3 20030224

AB ~~The invention relates to crystals of bicalutamide~~ having a specific crystal form, and industrially practicable **processes** for the production of bicalutamide and crystals thereof; these **processes** are excellent in environmental friendliness and economical efficiency. Bicalutamide was prepared by epoxidn. of N-methacryloyl-4-cyano-3-trifluoromethylaniline, followed by reaction with 4-fluorothiophenol, and oxidation

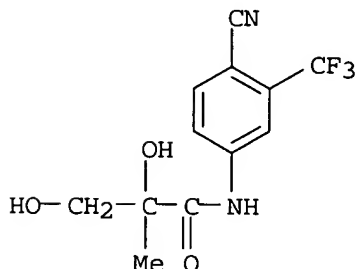
IT **316373-92-9P**

RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(preparation of bicalutamide in multi-step **process** starting from N-methacryloyl-4-cyano-3-trifluoromethylaniline and **process** for production of crystals of bicalutamide)

RN 316373-92-9 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-(9CI) (CA INDEX NAME)



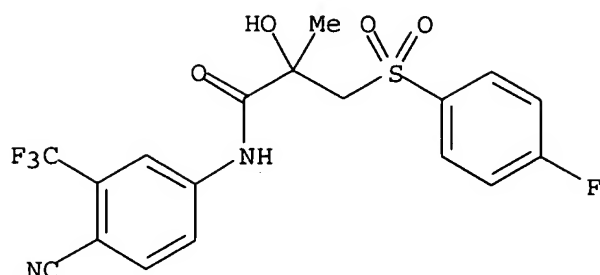
IT **90357-06-5P**, Bicalutamide

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of bicalutamide in multi-step **process** starting from N-methacryloyl-4-cyano-3-trifluoromethylaniline and **process** for production of crystals of bicalutamide)

RN 90357-06-5 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:300625 HCAPLUS

DOCUMENT NUMBER: 138:321017

TITLE: **Process** for making bicalutamide using a p-fluorobenzenesulfinic acid salt.

INVENTOR(S): Thijs, Lambertus; Keltjens, Rolf; Ettema, Gerrit Jan Bouke

PATENT ASSIGNEE(S): Synthon B.V., Neth.

SOURCE: U.S. Pat. Appl. Publ., 24 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003073742	A1	20030417	US 2002-261492	20021002
US 6818766--	B2	20041116		
WO 2004031136	A1	20040415	WO 2003-EP11166	20031001
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003273965	A1	20040423	AU 2003-273965	20031001
EP 1546093	A1	20050629	EP 2003-757932	20031001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004068135	A1	20040408	US 2003-682530	20031010
PRIORITY APPLN. INFO.:			US 2002-261492	A 20021002
			WO 2003-EP11166	W 20031001

OTHER SOURCE(S): CASREACT 138:321017; MARPAT 138:321017

AB Title **process** is claimed. Thus, N-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl-2-oxiranecarboxamide (preparation given), Na p-fluorobenzenesulfinate, and Bu4NBr were refluxed together for 96 h to give 48% bicalutamide.

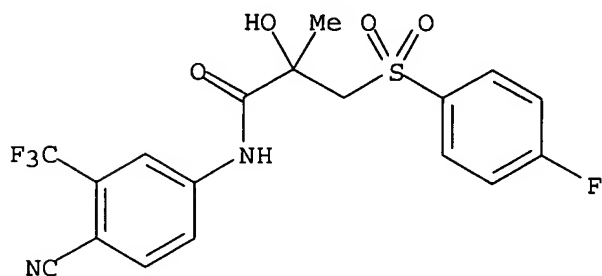
IT 90357-06-5P, Bicalutamide 113299-40-4P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(**process** for making bicalutamide using a p-fluorobenzenesulfinic acid salt)

RN 90357-06-5 HCAPLUS

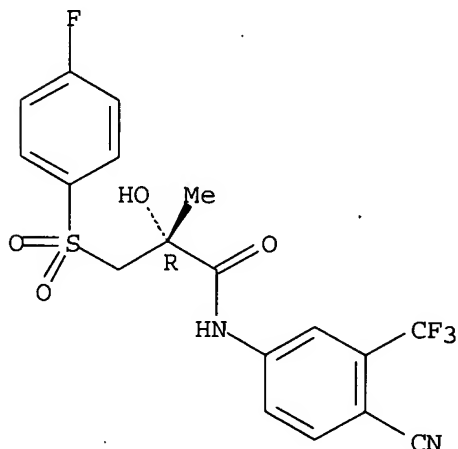
CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



RN 113299-40-4 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



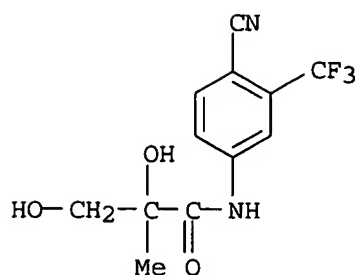
IT 316373-92-9P 316373-93-0P 316373-94-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(**process** for making bicalutamide using a p-fluorobenzenesulfinic acid salt)

RN 316373-92-9 HCAPLUS

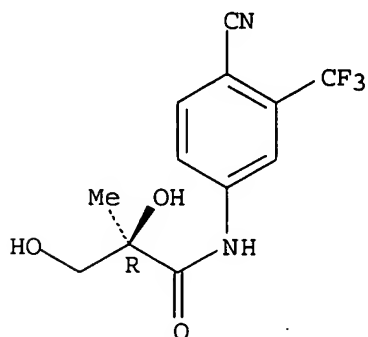
CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl- (9CI) (CA INDEX NAME)



RN 316373-93-0 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

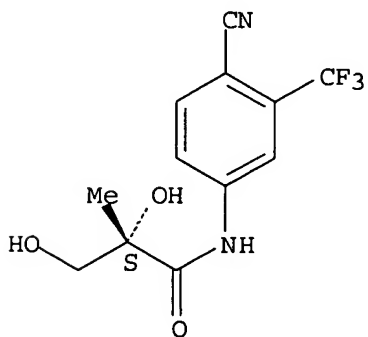
Absolute stereochemistry. Rotation (-).



RN 316373-94-1 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 18

THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 112 ibib abs hitstr tot

L12 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1274892 HCAPLUS

DOCUMENT NUMBER: 144:199095

TITLE: High-performance liquid chromatographic enantioseparation of bicalutamide and its related compounds

AUTHOR(S): Toeroek, Roland; Bor, Adam; Orosz, Gyoergy; Lukacs, Ferenc; Armstrong, Daniel W.; Peter, Antal

CORPORATE SOURCE: Department of Inorganic and Analytical Chemistry, University of Szeged, Szeged, H-6720, Hung.

SOURCE: Journal of Chromatography, A (2005), 1098(1-2), 75-81
CODEN: JCRAEY; ISSN: 0021-9673

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Direct high-performance liquid chromatog. methods were developed for the enantiosepn. of (R,S)-bicalutamide (1) and its analogs (\pm)-3-chloro-N-(4-cyano-3-(trifluoromethyl)phenyl)-2-hydroxy-2-methylpropanamide (2), (\pm)-N-(4-cyano-3-(trifluoro-methyl)phenyl)-2-methyloxirane-2-carboxamide (3), (\pm)-4-fluorophenylsulfonyl-2-hydroxy-2-methylpropionic acid (4), and (\pm)-3-hydroxy-N-(4-cyano-3-(trifluoromethyl)phenyl)-2-hydroxy-2-methylpropanamide (5). The methods involved the use of a cellulose-based Chiralcel OD-H, macrocyclic glycopeptide-based Chirobiotic T, TAG and R, β -cyclodextrin-based Cyclobond I 2000SN, and t-Bu carbamate-derivatized quinine-based columns. The conditions affording the best resolution were found by selection and variation of the mobile-phase compns., and the differences in separation capability of the methods were noted. The sequence of elution of the enantiomers was determined in all cases.

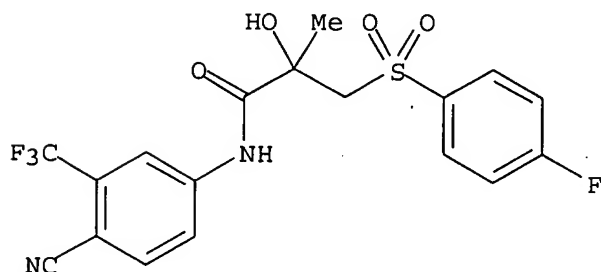
IT 90357-06-5, Bicalutamide 316373-92-9

RL: ANT (Analyte); ANST (Analytical study)

(HPLC enantiosepn. of bicalutamide and its related compds.)

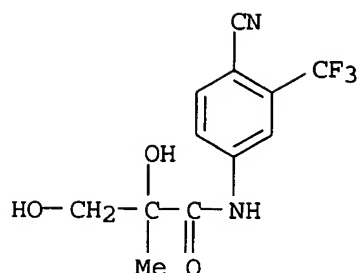
RN 90357-06-5 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



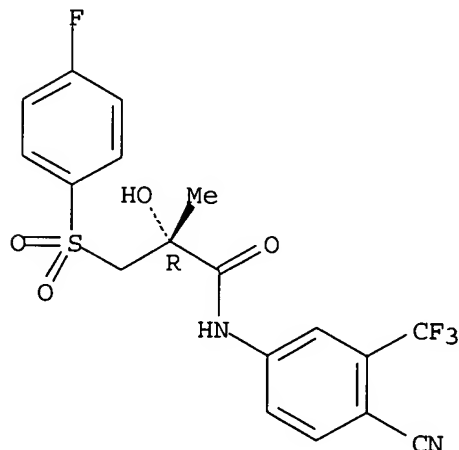
RN 316373-92-9 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl- (9CI) (CA INDEX NAME)



IT 113299-40-4, (R)-Bicalutamide
 RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (HPLC enantiosepn. of bicalutamide and its related compds.)
 RN 113299-40-4 HCAPLUS
 CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

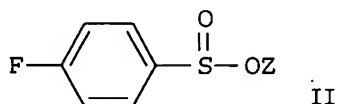
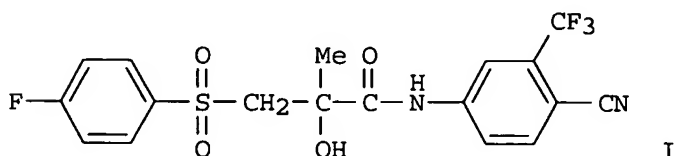
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:293441 HCAPLUS
 DOCUMENT NUMBER: 140:303414
 TITLE: Process for making bicalutamide and intermediates thereof
 INVENTOR(S): Thijs, Lambertus; Keltjens, Rolf; Ettema, Gerrit J. B.
 PATENT ASSIGNEE(S): Neth.
 SOURCE: U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U.S. Ser. No. 261,492.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004068135	A1	20040408	US 2003-682530	20031010
US 2003073742	A1	20030417	US 2002-261492	20021002
US 6818766	B2	20041116		
PRIORITY APPLN. INFO.:			US 2002-261492	A2 20021002
OTHER SOURCE(S):	MARPAT 140:303414			
GI				

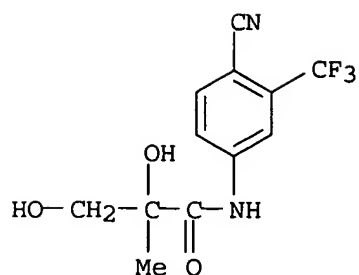


AB Bicalutamide (I) and/or its intermediates are made by reaction of p-fluorobenzenesulfinic acid salt (II; Z = a cation) with 2-hydroxyisobutyric acid derivs. of formula YCH₂C(Me)(OX)COA (A = OR; wherein R = H, C1-6 alkyl, C3-6 cycloalkyl, Ph, benzyl, 4-cyano-3-trifluoromethylphenyl; Y = leaving group and X = H; or X and Y are joined together to form a 3- to 6-membered heterocyclic ring, in particular oxirane ring; or X and A are joined together to form a 5- to 10-membered fused or unfused heterocyclic ring with the proviso that if a ring nitrogen is present, it may be substituted by a 3-trifluoromethyl-4-cyanophenyl group), YCH₂CMe:CH₂ (Y = same as above), or YCH₂CMe (Y = same as above). Thus, 0.500 g N-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl-2-oxiranecarboxamide (III) was dissolved in a mixture of 40 mL CHCl₃ and 40 mL H₂O, successively treated with 371 mg sodium p-fluorobenzenesulfinate and 298 mg tetrabutylammonium bromide, and refluxed for 96 h to give, after workup and silica gel chromatog., 380 mg I (48% yield). Similarly, chiral (R)-I was obtained using chiral epoxide (S)-III in 43% yield.

IT **316373-92-9P**, N-[4-Cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methylpropanamide **316373-93-0P**, N-[4-Cyano-3-(trifluoromethyl)phenyl]-(2R)-2,3-dihydroxy-2-methylpropanamide **316373-94-1P**, (2S)-N-[4-Cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methylpropanamide
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of bicalutamide by coupling of N-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl-2-oxiranecarboxamide or -3-(halo or mesyloxy)-2-hydroxy-2-methylpropanamide with sodium p-fluorobenzenesulfinate)

RN 316373-92-9 HCAPLUS

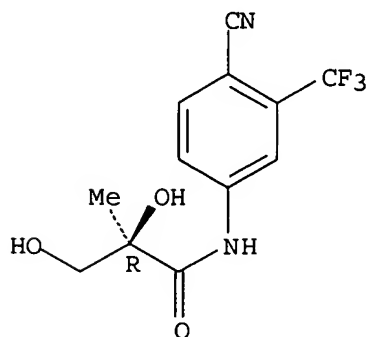
CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl- (9CI) (CA INDEX NAME)



RN 316373-93-0 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

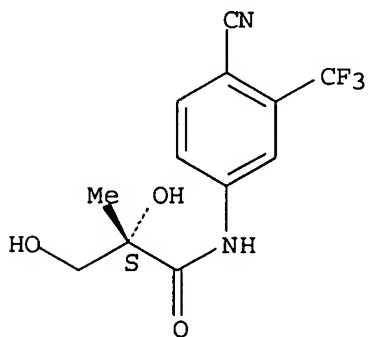
Absolute stereochemistry. Rotation (-).



RN 316373-94-1 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 90357-06-5P, Bicalutamide 113299-40-4P, (R)-Bicalutamide

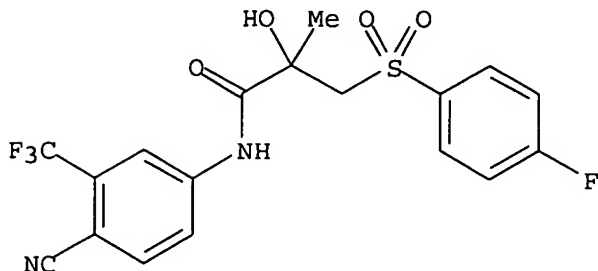
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of bicalutamide by coupling of N-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl-2-orixanecarboxamide or -3-(halo or mesyloxy)-2-hydroxy-2-methylpropanamide with sodium p-fluorobenzenesulfinate)

04/23/2006 1030665.trn

RN 90357-06-5 HCAPLUS

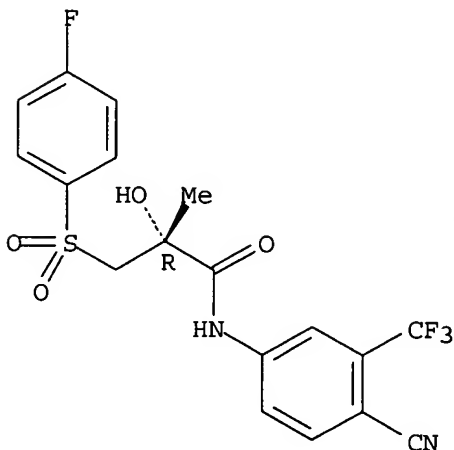
CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



RN 113299-40-4 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L12 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:511288 HCAPLUS

DOCUMENT NUMBER: 139:85122

TITLE: Process for preparing bicalutamide and crystals thereof

INVENTOR(S): ~~Shintaku~~, Tetsuya; Katsura, Tadashi; Itaya, Nobushige

PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053920	A1	20030703	WO 2002-JP13058	20021213

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2469594 AA 20030703 CA 2002-2469594 20021213

AU 2002354475 A1 20030709 AU 2002-354475 20021213

EP 1462442 A1 20040929 EP 2002-788815 20021213

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

BR 2002014933 A 20041214 BR 2002-14933 20021213

US 2003191337 A1 20031009 US 2003-362410 20030224

US 6740770 B2 20040525

US 2004133031 A1 20040708 US 2003-740140 20031218

ZA 2004004891 A 20050621 ZA 2004-4891 20040621

PRIORITY APPLN. INFO.:

JP 2001-380686 A 20011213

JP 2002-166213 A 20020606

WO 2002-JP13058 W 20021213

US 2003-362410 A3 20030224

AB The invention relates to crystals of bicalutamide having a specific crystal form, and industrially practicable processes for the production of bicalutamide and crystals thereof; these processes are excellent in environmental friendliness and economical efficiency. Bicalutamide was prepared by epoxidn. of N-methacryloyl-4-cyano-3-trifluoromethylaniline, followed by reaction with 4-fluorothiophenol, and oxidation

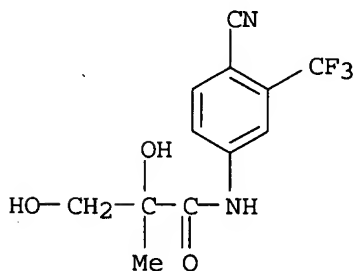
IT 316373-92-9P

RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(preparation of bicalutamide in multi-step process starting from N-methacryloyl-4-cyano-3-trifluoromethylaniline and process for production of crystals of bicalutamide)

RN 316373-92-9 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-(9CI) (CA INDEX NAME)



IT 90357-06-5P, Bicalutamide

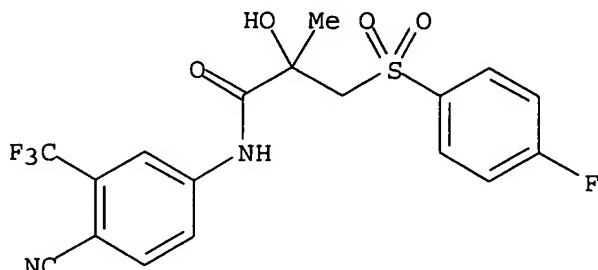
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of bicalutamide in multi-step process starting from

N-methacryloyl-4-cyano-3-trifluoromethylaniline and process for production of crystals of bicalutamide)

RN 90357-06-5 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:300625 HCAPLUS

DOCUMENT NUMBER: 138:321017

TITLE: Process for making bicalutamide using a p-fluorobenzenesulfinic acid salt.

INVENTOR(S): Thijs, Lambertus; Keltjens, Rolf; Ettema, Gerrit Jan Bouke

PATENT ASSIGNEE(S): Synthon B.V., Neth.

SOURCE: U.S. Pat. Appl. Publ., 24 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003073742	A1	200304117	US 2002-261492	20021002
US 6818766	B2	20041116		
WO 2004031136	A1	20040415	WO 2003-EP11166	20031001
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003273965	A1	20040423	AU 2003-273965	20031001
EP 1546093	A1	20050629	EP 2003-757932	20031001
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 2004068135	A1	20040408	US 2003-682530	20031010
PRIORITY APPLN. INFO.:			US 2002-261492	A 20021002
			WO 2003-EP11166	W 20031001

OTHER SOURCE(S): CASREACT 138:321017; MARPAT 138:321017

AB Title process is claimed. Thus, N-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl-2-oxiranecarboxamide (preparation given), Na p-fluorobenzenesulfinate, and Bu4NBr were refluxed together for 96 h to give 48% bicalutamide.

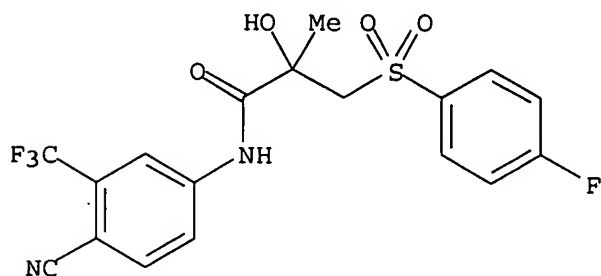
IT 90357-06-5P, Bicalutamide 113299-40-4P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for making bicalutamide using a p-fluorobenzenesulfinic acid salt)

RN 90357-06-5 HCAPLUS

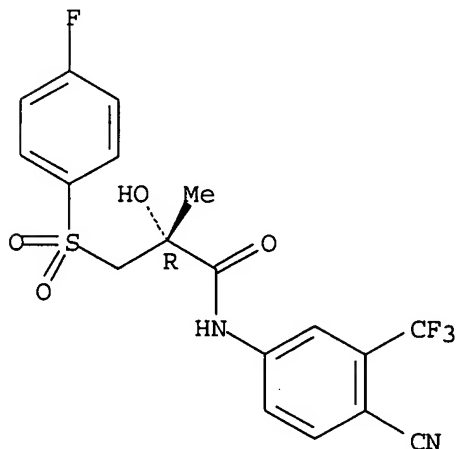
CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



RN 113299-40-4 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



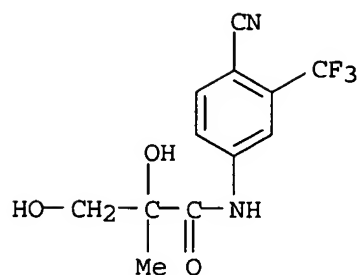
IT 316373-92-9P 316373-93-0P 316373-94-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(process for making bicalutamide using a p-fluorobenzenesulfinic acid salt)

RN 316373-92-9 HCAPLUS

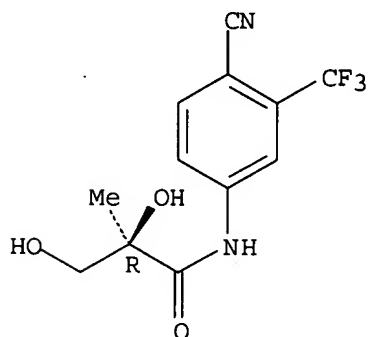
CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl- (9CI) (CA INDEX NAME)



RN 316373-93-0 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

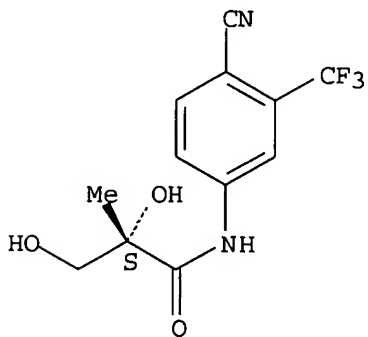
Absolute stereochemistry. Rotation (-).



RN 316373-94-1 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT:

18

THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:12441 HCAPLUS

DOCUMENT NUMBER: 134:86040

04/23/2006 1030665.trn

TITLE: Preparation of bicalutamide enantiomers
INVENTOR(S): Soros, Bela; Tuba, Zoltan; Galik, Gyorgy; Bor, Adam;
Demeter, Adam; Trischler, Ferenc; Horvath, Janos;
Balik, Janos
PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000608	A1	20010104	WO 2000-HU49	20000526
W: AE, AG, AL, AM, AT , AU, AZ , BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1189898	A1	20020327	EP 2000-937111	20000526
EP 1189898	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 234294	E	20030315	AT 2000-937111	20000526
ES 2188550	T3	20030701	ES 2000-937111	20000526
PRIORITY APPLN. INFO.:			HU 1999-1937	A 19990610
			WO 2000-HU49	W 20000526

OTHER SOURCE(S): CASREACT 134:86040

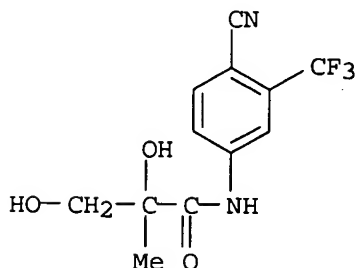
AB Racemic HOCH₂CMe(OH)CO₂H was optically resolved and the enantiomers treated with SOCL₂ to give the dioxathiolanonecarbonyl chloride which was amidated by H₂NC₆H₃(CF₃)(CN)-3,4. The deprotected dihydroxyamide was O-acylated by RSO₂Cl (R = 4-Me- or -BrC₆H₄) and the product thioetherified by 4-FC₆H₄SNa to give, after oxidation, the title compds.

IT 316373-92-9P 316373-93-0P 316373-94-1P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bicalutamide enantiomers)

RN 316373-92-9 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-
(9CI) (CA INDEX NAME)

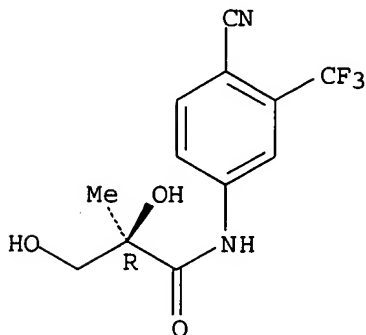


04/23/2006 1030665.trn

RN 316373-93-0 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

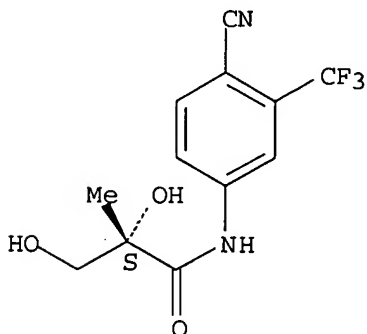
Absolute stereochemistry. Rotation (-).



RN 316373-94-1 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



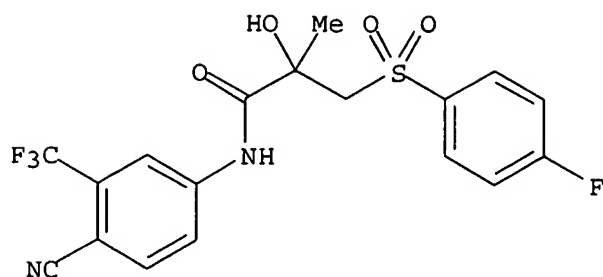
IT 90357-06-5P 113299-38-0P 113299-40-4P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of bicalutamide enantiomers)

RN 90357-06-5 HCAPLUS

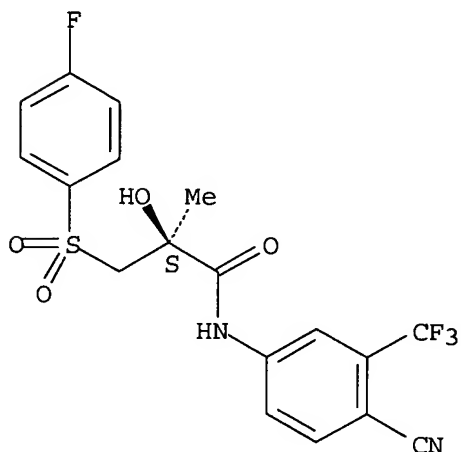
CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl- (9CI) (CA INDEX NAME)



RN 113299-38-0 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

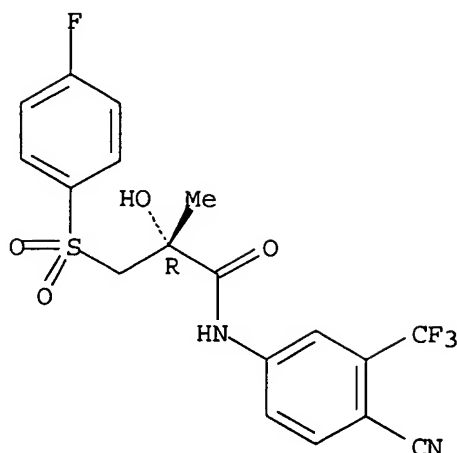
Absolute stereochemistry. Rotation (+).



RN 113299-40-4 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l11 ibib abs hitstr tot

L11 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1274892 HCAPLUS

DOCUMENT NUMBER: 144:199095

TITLE: High-performance liquid chromatographic enantioseparation of bicalutamide and its related compounds

AUTHOR(S): Toeroek, Roland; Bor, Adam; Orosz, Gyoergy; Lukacs, Ferenc; Armstrong, Daniel W.; Peter, Antal

CORPORATE SOURCE: Department of Inorganic and Analytical Chemistry, University of Szeged, Szeged, H-6720, Hungary

SOURCE: Journal of Chromatography, A (2005), 1098(1-2), 75-81
CODEN: JCRAEY; ISSN: 0021-9673

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Direct high-performance liquid chromatog. methods were developed for the enantiosepn. of (R,S)-bicalutamide (1) and its analogs (±)-3-chloro-N-(4-cyano-3-(trifluoromethyl)phenyl)-2-hydroxy-2-methylpropanamide (2), (±)-N-(4-cyano-3-(trifluoro-methyl)phenyl)-2-methyloxirane-2-carboxamide (3), (±)-4-fluorophenylsulfonyl-2-hydroxy-2-methylpropionic acid (4), and (±)-3-hydroxy-N-(4-cyano-3-(trifluoromethyl)phenyl)-2-hydroxy-2-methylpropanamide (5). The methods involved the use of a cellulose-based Chiralcel OD-H, macrocyclic glycopeptide-based Chirobiotic T, TAG and R, β-cyclodextrin-based Cyclobond I 2000SN, and t-Bu carbamate-derivatized quinine-based columns. The conditions affording the best resolution were found by selection and variation of the mobile-phase compns., and the differences in separation capability of the methods were noted. The sequence of elution of the enantiomers was determined in all cases.

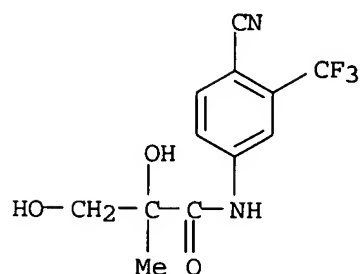
IT 316373-92-9

RL: ANT (Analyte); ANST (Analytical study)
(HPLC enantiosepn. of bicalutamide and its related compds.)

RN 316373-92-9 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-

(9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:293441 HCAPLUS

DOCUMENT NUMBER: 140:303414

TITLE: Process for making bicalutamide and intermediates thereof

INVENTOR(S): Thijs, Lambertus; Keltjens, Rolf; Ettema, Gerrit J. B. Neth.

PATENT ASSIGNEE(S):

SOURCE: U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U.S. Ser. No. 261,492.

CODEN: USXXCO

DOCUMENT TYPE: Patent

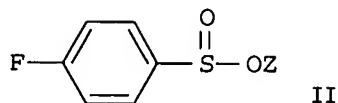
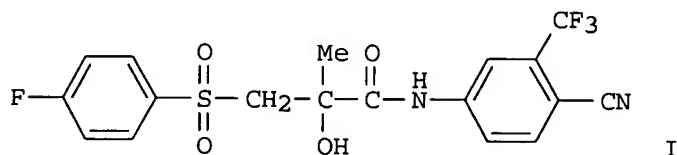
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004068135	A1	20040408	US 2003-682530	20031010
US 2003073742	A1	20030417	US 2002-261492	20021002
US 6818766	B2	20041116		
PRIORITY APPLN. INFO.:			US 2002-261492	A2 20021002
OTHER SOURCE(S):		MARPAT 140:303414		

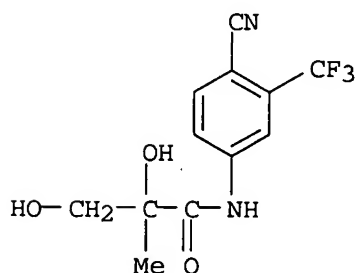
GI



AB Bicalutamide (I) and/or its intermediates are made by reaction of p-fluorobenzenesulfinic acid salt (II; Z = a cation) with

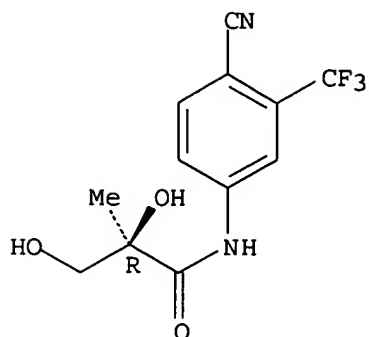
2-hydroxyisobutyric acid derivs. of formula $YCH_2C(Me)(OX)COA$ ($A = OR$; wherein $R = H$, C1-6 alkyl, C3-6 cycloalkyl, Ph, benzyl, 4-cyano-3-trifluoromethylanilino; $Y =$ leaving group and $X = H$; or X and Y are joined together to form a 3- to 6-membered heterocyclic ring, in particular oxirane ring; or X and A are joined together to form a 5- to 10-membered fused or unfused heterocyclic ring with the proviso that if a ring nitrogen is present, it may be substituted by a 3-trifluoromethyl-4-cyanophenyl group), $YCH_2CMe:CH_2$ ($Y =$ same as above), or $YCH_2C(OMe)$ ($Y =$ same as above). Thus, 0.500 g N-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl-2-oxiranecarboxamide (III) was dissolved in a mixture of 40 mL $CHCl_3$ and 40 mL H_2O , successively treated with 371 mg sodium p-fluorobenzenesulfinate and 298 mg tetrabutylammonium bromide, and refluxed for 96 h to give, after workup and silica gel chromatog., 380 mg I (48% yield). Similarly, chiral (R)-I was obtained using chiral epoxide (S)-III in 43% yield.

IT **316373-92-9P**, N-[4-Cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methylpropanamide **316373-93-0P**, N-[4-Cyano-3-(trifluoromethyl)phenyl]-(2R)-2,3-dihydroxy-2-methylpropanamide **316373-94-1P**, (2S)-N-[4-Cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methylpropanamide
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of bicalutamide by coupling of N-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl-2-oxiranecarboxamide or -3-(halo or mesyloxy)-2-hydroxy-2-methylpropanamide with sodium p-fluorobenzenesulfinate)
 RN **316373-92-9** HCAPLUS
 CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-(9CI) (CA INDEX NAME)



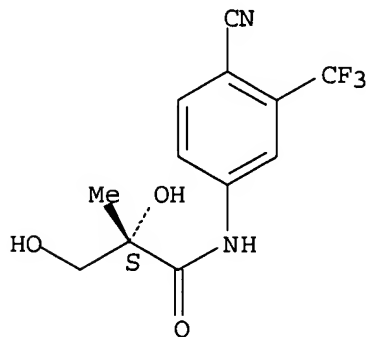
RN **316373-93-0** HCAPLUS
 CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 316373-94-1 HCAPLUS
 CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:511288 HCAPLUS
 DOCUMENT NUMBER: 139:85122
 TITLE: Process for preparing bicalutamide and crystals thereof
 INVENTOR(S): Shintaku, Tetsuya; Katsura, Tadashi; Itaya, Nobushige
 PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 46 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053920	A1	20030703	WO 2002-JP13058	20021213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2469594 AA 20030703 CA 2002-2469594 20021213
 AU 2002354475 A1 20030709 AU 2002-354475 20021213
 EP 1462442 A1 20040929 EP 2002-788815 20021213

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

BR 2002014933 A 20041214 BR 2002-14933 20021213
 US 2003191337 A1 20031009 US 2003-362410 20030224
 US 6740770 B2 20040525
 US 2004133031 A1 20040708 US 2003-740140 20031218
 ZA 2004004891 A 20050621 ZA 2004-4891 20040621

PRIORITY APPLN. INFO.:

JP 2001-380686 A 20011213
 JP 2002-166213 A 20020606
 WO 2002-JP13058 W 20021213
 US 2003-362410 A3 20030224

AB The invention relates to crystals of bicalutamide having a specific crystal form, and industrially practicable processes for the production of bicalutamide and crystals thereof; these processes are excellent in environmental friendliness and economical efficiency. Bicalutamide was prepared by epoxidn. of N-methacryloyl-4-cyano-3-trifluoromethylaniline, followed by reaction with 4-fluorothiophenol, and oxidation

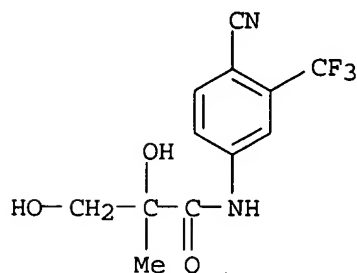
IT 316373-92-9P

RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(preparation of bicalutamide in multi-step process starting from N-methacryloyl-4-cyano-3-trifluoromethylaniline and process for production of crystals of bicalutamide)

RN 316373-92-9 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-(9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:300625 HCAPLUS

DOCUMENT NUMBER: 138:321017

TITLE: Process for making bicalutamide using a p-fluorobenzenesulfinic acid salt.

INVENTOR(S): Thijs, Lambertus; Keltjens, Rolf; Ettema, Gerrit Jan Bouke

PATENT ASSIGNEE(S): Synthon B.V., Neth.

SOURCE: U.S. Pat. Appl. Publ., 24 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003073742	A1	20030417	US 2002-261492	20021002
US 6818766	B2	20041116		
WO 2004031136	A1	20040415	WO 2003-EP11166	20031001
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003273965	A1	20040423	AU 2003-273965	20031001
EP 1546093	A1	20050629	EP 2003-757932	20031001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004068135	A1	20040408	US 2003-682530	20031010
PRIORITY APPLN. INFO.:			US 2002-261492	A 20021002
			WO 2003-EP11166	W 20031001

OTHER SOURCE(S): CASREACT 138:321017; MARPAT 138:321017

AB Title process is claimed. Thus, N-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl-2-oxiranecarboxamide (preparation given), Na p-fluorobenzenesulfinate, and Bu4NBr were refluxed together for 96 h to give 48% bicalutamide.

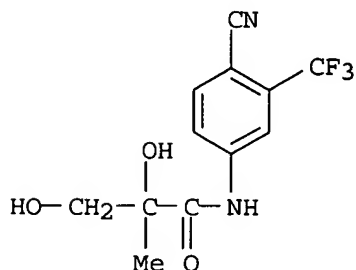
IT 316373-92-9P 316373-93-0P 316373-94-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(process for making bicalutamide using a p-fluorobenzenesulfinic acid salt)

RN 316373-92-9 HCAPLUS

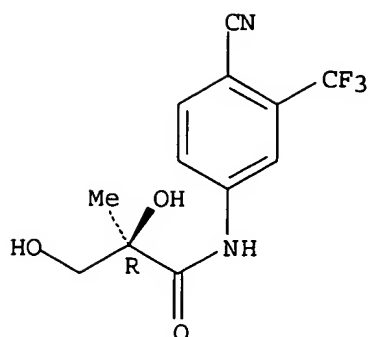
CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-(9CI) (CA INDEX NAME)



RN 316373-93-0 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

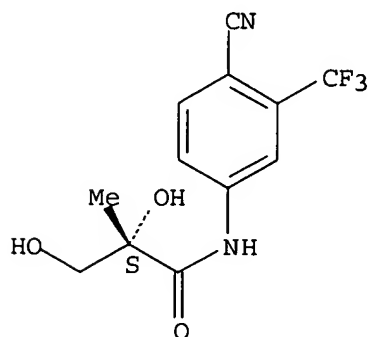
Absolute stereochemistry. Rotation (-).



RN 316373-94-1 HCAPLUS

CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:12441 HCAPLUS

DOCUMENT NUMBER: 134-86040

TITLE: Preparation of bicalutamide enantiomers

INVENTOR(S): Soros, Bela; Tuba, Zoltan; Galik, Gyorgy; Bor, Adam; Demeter, Adam; Trischler, Ferenc; Horvath, Janos; Brlik, Janos

PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

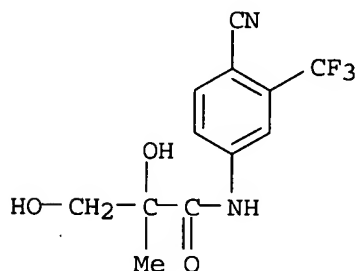
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

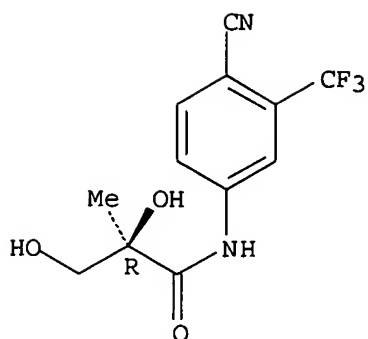
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000608	A1	20010104	WO 2000-HU49	20000526
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LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
 SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
 ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 EP 1189898 A1 20020327 EP 2000-937111 20000526
 EP 1189898 B1 20030312
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO
 AT 234294 E 20030315 AT 2000-937111 20000526
 ES 2188550 T3 20030701 ES 2000-937111 20000526
 PRIORITY APPLN. INFO.: HU 1999-1937 A 19990610
 WO 2000-HU49 W 20000526
 OTHER SOURCE(S): CASREACT 134:86040
 AB Racemic HOCH₂CMe(OH)CO₂H was optically resolved and the enantiomers
 treated with SOCl₂ to give the dioxathiolanonecarbonyl chloride which was
 amidated by H₂NC₆H₃(CF₃)(CN)-3,4. The deprotected dihydroxyamide was
 O-acylated by RSO₂Cl (R = 4-Me- or -BrC₆H₄) and the product thioetherified
 by 4-FC₆H₄SNa to give, after oxidation, the title compds.
 IT **316373-92-9P 316373-93-0P 316373-94-1P**
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic
 preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of bicalutamide enantiomers)
 RN 316373-92-9 HCAPLUS
 CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-
 (9CI) (CA INDEX NAME)



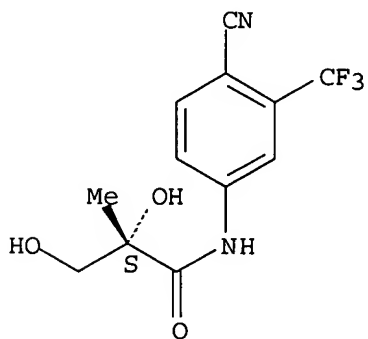
RN 316373-93-0 HCAPLUS
 CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-
 , (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 316373-94-1 HCAPLUS
 CN Propanamide, N-[4-cyano-3-(trifluoromethyl)phenyl]-2,3-dihydroxy-2-methyl-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE	TOTAL
ENTRY	SESSION
74.02	469.08
SINCE FILE	TOTAL
ENTRY	SESSION
-9.75	-13.50

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